WHAT IS CLAIMED IS:

1. A ligand that binds specifically to a region of a polymeric immunoglobulin receptor (pIgR) of a cell of an animal, which pIgR when cleaved has a stalk region which remains attached to the cell and a secretory component (SC) which exists in an organ of interest in several forms, provided that the ligand does not substantially bind to the most abundant form of SC present in the organ of interest and provided further that the ligand does not substantially bind to the stalk of said pIgR under physiological conditions.

2. A ligand of claim 1 in which the animal is a bird.

3. A ligand of claim 1 in which the animal is a mammal.

4 A ligand of claim 3 in which the mammal is selected from the group consisting of pig, cow, horse, sheep, goat, cat, dog, and human.

5. A ligand of claim 1 wherein the ligand is an antibody.

6. A ligand of claim 1 wherein the ligand is a humanized antibody.

7. A ligand of claim 1 wherein the ligand is selected from the group consisting of a recombinant single chain variable region fragment of an antibody and a disulfide stabilized variable region fragment.

8. A ligand of claim 1 which binds to a peptide derived from human pIgR (SEQ ID NO:2), which peptide is selected from the group consisting of: Lys487-Arg603, Lys487-Glu607, Lys487-Val611, Lys487-Arg615, Lys487-Ala618, Cys520-Arg603, Cys520-Glu607, Cys520-Val611, Cys520-Arg615, Cys520-Ala618, Lys577-Arg603, Lys577-Glu607, Lys577-Val611, Lys577-Arg615, Lys577-Ala618, Ser574-Arg603, Ser574-Glu607, Ser574-Val611, Ser574-Arg615, Ser574-Ala618, Val560-Arg603, Val560-Glu607, Val560-Val611, Val560-Arg615, Val560-Ala618, Cys544-Arg603, Cys544-Glu607, Cys544-Val611, Cys544-Arg615, and Cys544-Ala618.

9. The ligand of claim 1, further wherein the ligand binds to an epitope selected from the group consisting of QDPRLF (SEQ ID NO:10), LDPRLF (SEQ ID NO:11), KAIQDPRLF (SEQ ID NO:12), LDPRLFADERI (SEQ ID NO:13),

DENKANLDPRLF (SEQ ID NO:14), RLFADEREI (SEQ ID NO:15), and LDPRLFADE (SEQ ID NO:16).

10. The ligand of claim 1, wherein the organ of interest is selected from the group consisting of a small intestine, a large intestine, a liver-biliary tree, a salivary gland, a stomach, a lung, a vagina, a uterus, a lacrimal gland, a mammary gland, a nasal passage, and a sinus.

11. A ligand of claim 1 which is further defined as comprising a binding component for binding to pIgR and a biologically active component.

12. A ligand of claim 11, wherein the organ of interest is the lung.

13. A ligand of claim 12, wherein the biologically active component is a nucleic acid encoding the wildtype cystic fibrosis transmembrane conductance regulator.

14. A ligand of claim 11, wherein the biologically active component is selected from the group consisting of a nucleic acid, a protein, a radioisotope, a lipid, a carbohydrate, a peptidomimetic, an anti-inflammatory, an antibiotic, and an anti-infective.

15. A ligand of claim 11, wherein the biologically active component is a small molecule.

16. A ligand that binds specifically to a region of a polymeric immunoglobulin receptor (pIgR) of a cell of an animal, which pIgR has an initial cleavage site and which upon initial cleavage has a stalk region which remains attached to the cell and a secretory component (SC) which exists in an organ of interest in several forms, provided that the ligand does not substantially bind to the most abundant form of SC present in the organ of interest and provided further that the ligand does not substantially bind to a peptide comprising 31 amino acids that are cell-membrane-proximal to the initial cleavage site.

17. A method of introducing a ligand into a cell of an organ of interest in an animal, which cell expresses a polymeric immunoglobulin receptor, by binding the ligand to a region of the polymeric immunoglobulin receptor, with the provisos that

(a) the ligand does not substantially bind to a form of secretory component

which is the most abundant form present in the organ of interest under physiological conditions and

(b) the ligand does not substantially bind to a stalk region of the pIgR, thereby permitting introduction of the ligand into the cell.

18. A method of claim 17, wherein the ligand is an antibody.

19. A method of claim 17, wherein the ligand is a humanized antibody.

20. A method of claim 17, wherein the ligand is selected from the group consisting of a recombinant single chain variable region fragment of an antibody and a disulfide stabilized variable region fragment.

21. A method of claim 17, wherein the ligand selectively binds to a peptide derived from human pIgR (SEQ ID NO:2), which peptide is selected from the group consisting of: Lys487-Arg603, Lys487-Glu607, Lys487-Val611, Lys487-Arg615, Lys487-Ala618, Cys520-Arg603, Cys520-Glu607, Cys520-Val611, Cys520-Arg615, Cys520-Ala618, Lys577-Arg603, Lys577-Glu607, Lys577-Val611, Lys577-Arg615, Lys577-Ala618, Ser574-Arg603, Ser574-Glu607, Ser574-Val611, Ser574-Arg615, Ser574-Ala618, Val560-Arg603, Val560-Glu607, Val560-Val611, Val560-Arg615, Val560-Ala618, Cys544-Arg603, Cys544-Glu607, Cys544-Val611, Cys544-Arg615, and Cys544-Ala618.

22. The method of claim 17, wherein the ligand binds to an epitope selected from the group consisting of QDPRLF (SEQ ID NO:10), LDPRLF (SEQ ID NO:11), KAIQDPRLF (SEQ ID NO:12), LDPRLFADERI (SEQ ID NO:13), DENKANLDPRLF (SEQ ID NO:14), RLFADEREI (SEQ ID NO:15), and LDPRLFADE (SEQ ID NO:16).

23. A method of claim 17, wherein the ligand is further defined as having a binding component for selectively binding to pIgR and a biologically active component.

24. A method of claim 23, wherein the biologically active component is a nucleic acid which encodes the wildtype cystic fibrosis transmembrane conductance regulator.

25. A method of claim 17, wherein the biologically active component is selected from the group consisting of a nucleic acid, a protein, a radioisotope, a lipid, a carbohydrate, a peptidomimetic, an anti-inflammatory, an antibiotic, and an anti-infective.

26. A method of claim 17, wherein the biologically active component is a small molecule.

27. A method of claim 17, wherein the cell is a mammalian cell.

28. A method of claim 27, wherein the cell is an epithelial cell.

29. A method of claim 17, wherein the organ of interest is selected from the group consisting of a small intestine, a large intestine, a liver-biliary tree, a stomach, a salivary gland, a lung, a vagina, a uterus, a lacrimal gland, a mammary gland, a nasal passage, and a sinus.

30. A method of introducing a ligand into a cell of an organ of interest in an animal, which cell expresses a polymeric immunoglobulin receptor (pIgR), which pIgR has an initial cleavage site which, upon initial cleavage has a stalk region, the method comprising binding the ligand to a region of the pIgR, with the provisos that

(a) the ligand does not substantially bind to a form of secretory component which is the most abundant form present in the organ of interest under physiological conditions;

(b) the ligand does not substantially bind to a stalk region of the pIgR; and

(c) the ligand does not bind to an extracellular epitope within the first 31 amino acids that are cell membrane proximal to the initial cleavage site of the pIgR, thereby permitting introduction of the ligand into the cell.

31. A method of increasing the rate by which a first ligand which binds to secretory component (SC) is internalized into a cell secreting a polymeric immunoglobulin receptor (pIgR) from an apical surface by

(a) binding the pIgR with a second ligand, which second ligand inhibits proteolytic cleavage of SC by at least one-third, and further which second ligand does not substantially bind to a stalk remaining attached to the cell after proteolytic cleavage, and

(b) binding the first ligand to the SC,

thereby permitting internalization into said cell of the SC to which the first ligand is bound.

32 A ligand that binds specifically to a region of a polymeric immunoglobulin receptor (pIgR) of a cell, provided that binding of the ligand reduces proteolytic cleavage of secretory component (SC) by at least one-third compared to the cleavage of SC from a cell in the absence of binding of the ligand and provided further that the ligand does not substantially bind to a stalk of said pIgR remaining after proteolytic cleavage under physiological conditions.

33. A ligand of claim 32, wherein the ligand is an antibody.

34. A ligand of claim 33, wherein the ligand is a humanized antibody.

35. A ligand of claim 33, wherein the ligand is a scFv.

36. A ligand of claim 33, wherein the ligand is selected from the group consisting of a recombinant single chain variable region fragment of an antibody and a disulfide stabilized variable region fragment.

37. A ligand of claim 32, which binds to a peptide derived from human pIgR (SEQ ID NO:2), selected from the group consisting of: Lys487-Arg603, Lys487-Glu607, Lys487-Val611, Lys487-Arg615, Lys487-Ala618, Cys520-Arg603, Cys520-Glu607, Cys520-Val611, Cys520-Arg615, Cys520-Ala618, Lys577-Arg603, Lys577-Glu607, Lys577-Val611, Lys577-Arg615, Lys577-Ala618, Ser574-Arg603, Ser574-Glu607, Ser574-Val611, Ser574-Arg615, Ser574-Ala618, Val560-Arg603, Val560-Glu607, Val560-Val611, Val560-Arg615, Val560-Ala618, Cys544-Arg603, Cys544-Glu607, Cys544-Val611, Cys544-Arg615, and Cys544-Ala618.

38. The ligand of claim 32, wherein the ligand binds to an epitope selected from the group consisting of QDPRLF (SEQ ID NO:10), LDPRLF (SEQ ID NO:11), KAIQDPRLF (SEQ ID NO:12), LDPRLFADERI (SEQ ID NO:13), DENKANLDPRLF (SEQ ID NO:14), RLFADEREI (SEQ ID NO:15), and LDPRLFADE (SEQ ID NO:16).

39 A ligand of claim 32 which is further defined as a binding component of a molecule comprising a biologically active component.

40. A ligand of claim 39, wherein said biologically active component is selected from the group consisting of: a nucleic acid, a protein, a radioisotope, a lipid, a carbohydrate, a peptidomimetic, an anti-inflammatory, an antibiotic, and an anti-infective.

41. A ligand of claim 39, wherein the biologically active component is a small molecule.

42. A ligand of claim 39, wherein the biologically active component is a nucleic acid encoding the wildtype cystic fibrosis transmembrane conductance regulator.

43. A conjugate, fusion protein, or complex, said conjugate fusion protein or complex comprising a ligand that binds specifically to a region of a polymeric immunoglobulin receptor (pIgR) of a cell and a biologically active component, provided that binding of the conjugate, fusion protein, or complex to pIgR reduces proteolytic cleavage of secretory component (SC) by at least one-third compared to the cleavage of SC from a cell in the absence of binding of the conjugate, fusion protein, or complex and provided further that the conjugate, fusion protein, or complex does not substantially bind to a stalk of said pIgR remaining after proteolytic cleavage under physiological conditions.

44. A method of introducing a ligand into a cell expressing a polymeric immunoglobulin receptor (pIgR) by attaching the ligand to a region of the pIgR, provided that

(a) binding of the ligand reduces proteolytic cleavage of secretory component (SC) by at least one-third compared to the cleavage of SC from a cell in the absence of the ligand, and

(b) the ligand does not substantially bind to a stalk of said pIgR remaining after proteolytic cleavage under physiological conditions,

thereby permitting introduction of the ligand into the cell.

45. A method of claim 44, wherein the ligand is an antibody.

46. A method of claim 45, wherein the ligand is a humanized antibody.

47. A method of claim 45, wherein the ligand is a scFv.

48. A method of claim 45, wherein the ligand is selected from the group consisting of a recombinant single chain variable region fragment of an antibody and a disulfide stabilized variable region.

49. A method of claim 44, wherein the ligand binds to a peptide derived from human pIgR (SEQ ID NO:2), selected from the group consisting of: Lys487-Arg603, Lys487-Glu607, Lys487-Val611, Lys487-Arg615, Lys487-Ala618, Cys520-Arg603, Cys520-Glu607, Cys520-Val611, Cys520-Arg615, Cys520-Ala618, Lys577-Arg603, Lys577-Glu607, Lys577-Val611, Lys577-Arg615, Lys577-Ala618, Ser574-Arg603, Ser574-Glu607, Ser574-Val611, Ser574-Arg615, Ser574-Ala618, Val560-Arg603, Val560-Glu607, Val560-Val611, Val560-Arg615, Val560-Ala618, Cys544-Arg603, Cys544-Glu607, Cys544-Val611, Cys544-Arg615, and Cys544-Ala618.

50. The method of claim 44, wherein the ligand binds to an epitope of pIgR selected from the group consisting of QDPRLF (SEQ ID NO:10), LDPRLF (SEQ ID NO:11), KAIQDPRLF (SEQ ID NO:12), LDPRLFADERI (SEQ ID NO:13), DENKANLDPRLF (SEQ ID NO:14), RLFADEREI (SEQ ID NO:15), and LDPRLFADE (SEQ ID NO:16).

51. A method of claim 44, wherein the ligand is further defined as having a binding component for selectively binding to a region of pIgR and a biologically active component.

52. The method of claim 51, wherein the biologically active component is selected from the group consisting of: a nucleic acid, a protein, a radioisotope, a lipid, a carbohydrate, a peptidomimetic, an anti-inflammatory, an antibiotic, and an anti-infective.

53. The method of claim 51, wherein the biologically active component is a small molecule.

54. A method of claim 51, wherein the animal is a mammal.

55. A method of claim 51, wherein the biologically active component is a nucleic acid encodes the wildtype cystic fibrosis transmembrane conductance regulator.

56. A method of claim 44, wherein the cell is a mammalian cell.

57. A method of claim 56, wherein the cell is an epithelial cell.

58. The method of claim 44, wherein the ligand binds to the pIgR at the apical surface of the cell.

59. The method of claim 59, wherein the ligand is transcytosed to the basolateral side of the cell.

60. The method of claim 59, wherein the ligand is released from the pIgR at the basolateral surface of the cell.

61. The method of claim 44, wherein the ligand is attached to the pIgR at the basolateral surface of the cell.

62. The method of claim 44, wherein the SC exists in several forms in an organ of interest, and provided that the ligand

(a) does not bind to the most abundant form of SC present in the organ of interest, and

(b) does not bind to a stalk remaining on an extracellular surface of a cell of the organ of interest after pIgR cleavage.

63. The method of claim 62, wherein the organ of interest is selected from the group consisting of a small intestine, a large intestine, a liver-biliary tree, a stomach, a salivary gland, a lung, a vagina, a uterus, a lacrimal gland, a mammary gland, a nasal passage, and a sinus.

64. A method of attaching a ligand to a cell expressing a polymeric immunoglobulin receptor comprising the step of binding the ligand to the receptor with the provisos that

(a) the ligand reduces proteolytic cleavage of secretory component (SC) by at least one-third compared to the cleavage of SC from a cell in the absence of the ligand, and

(b) the ligand does not substantially bind to a stalk of said pIgR remaining

after proteolytic cleavage under physiological conditions,
thereby attaching the ligand to the cell.

65. The method of claim 64, wherein the ligand is internalized into the cell after binding.

66. A method of attaching a conjugate, fusion protein, or complex to a cell expressing a polymeric immunoglobulin receptor, said conjugate, fusion protein, or complex comprising a ligand that binds to a region of pIgR and a biologically active component, said method comprising the step of binding the ligand to the receptor with the provisos that

(a) the ligand reduces proteolytic cleavage of secretory component (SC) by at least one-third compared to the cleavage of SC from a cell in the absence of the ligand, and

(b) the ligand does not substantially bind to a stalk of said pIgR remaining after proteolytic cleavage under physiological conditions,
thereby attaching the conjugate, fusion protein, or complex to the cell.

67. A method of transcytosing a ligand from an apical to a basolateral side of a cell of an organ of interest in an animal, which cell expresses a polymeric immunoglobulin receptor (pIgR), by binding the ligand to a region of the polymeric immunoglobulin receptor, with the provisos that

(a) the ligand does not substantially bind to a form of secretory component which is the most abundant form present in the organ of interest under physiological conditions and

(b) the ligand does not substantially bind to a stalk region of the pIgR, thereby permitting introduction of the ligand into the cell.

68. A method of claim 67, wherein the ligand is an antibody.

69. A method of claim 68, wherein the ligand is a humanized antibody.

70. A method of claim 67, wherein the ligand is selected from the group consisting of a recombinant single chain variable region fragment of an antibody and a disulfide stabilized variable region fragment.

71. A method of claim 67, wherein the ligand selectively binds to a peptide derived from human pIgR (SEQ ID NO:2), which peptide is selected from the group consisting of: Lys487-Arg603, Lys487-Glu607, Lys487-Val611, Lys487-Arg615, Lys487-Ala618, Cys520-Arg603, Cys520-Glu607, Cys520-Val611, Cys520-Arg615, Cys520-Ala618, Lys577-Arg603, Lys577-Glu607, Lys577-Val611, Lys577-Arg615, Lys577-Ala618, Ser574-Arg603, Ser574-Glu607, Ser574-Val611, Ser574-Arg615, Ser574-Ala618, Val560-Arg603, Val560-Glu607, Val560-Val611, Val560-Arg615, Val560-Ala618, Cys544-Arg603, Cys544-Glu607, Cys544-Val611, Cys544-Arg615, and Cys544-Ala618.

72. The method of claim 67, wherein the ligand binds to an epitope selected from the group consisting of QDPRLF (SEQ ID NO:10), LDPRLF (SEQ ID NO:11), KAIQDPRLF (SEQ ID NO:12), LDPRLFADERI (SEQ ID NO:13), DENKANLDPRLF (SEQ ID NO:14), RLFADERRI (SEQ ID NO:15), and LDPRLFADE (SEQ ID NO:16).

73. A method of claim 67 wherein the ligand is further defined as having a binding component for selectively binding to pIgR and a biologically active component.

74. A method of claim 73, wherein the biologically active component is selected from the group consisting of a nucleic acid, a peptide, a protein, a radioisotope, a lipid, a carbohydrate, a peptidomimetic, an anti-inflammatory, an antisense oligonucleotide, an antibiotic, and an anti-infective.

75. A method of claim 73, wherein the biologically active component is a small molecule

76. A method of claim 67, wherein the cell is a mammalian cell.

77. A method of claim 76, wherein the cell is an epithelial cell.

78. A method of claim 67, wherein the organ of interest is selected from the group consisting of a small intestine, a large intestine, a liver-biliary tree, a stomach, a salivary gland, a lung, a vagina, a uterus, a lacrimal gland, a mammary gland, a nasal passage, and a sinus.

79. A method of transcytosing a ligand from an apical to a basolateral side of a cell of an organ of interest in an animal, which cell expresses a polymeric immunoglobulin receptor (pIgR), which pIgR has an initial cleavage site which, upon initial cleavage has a stalk region, the method comprising binding the ligand to a region of the pIgR, with the provisos that

(a) the ligand does not substantially bind to a form of secretory component which is the most abundant form present in the organ of interest under physiological conditions;

(b) the ligand does not substantially bind to a stalk region of the pIgR; and

(c) the ligand does not bind to an extracellular epitope within the first 31 amino acids that are cell membrane proximal to the initial cleavage site of the pIgR,

thereby permitting introduction of the ligand into the cell.

80. A method of transcytosing a ligand from an apical to a basolateral side of a cell of an organ of interest in an animal, which cell expresses a polymeric immunoglobulin receptor (pIgR),by attaching the ligand to a region of the pIgR, provided that

(a) binding of the ligand reduces proteolytic cleavage of secretory component (SC) by at least one-third compared to the cleavage of SC from a cell in the absence of the ligand, and

(b) the ligand does not substantially bind to a stalk of said pIgR remaining after proteolytic cleavage under physiological conditions,

thereby permitting transcytosis of the ligand from the apical side to the basolateral side of the cell.

81. A method of claim 80, wherein the ligand is an antibody.

82. A method of claim 81, wherein the ligand is a humanized antibody.

83. A method of claim 81, wherein the ligand is a scFv.

84. A method of claim 80, wherein the ligand is selected from the group consisting of a recombinant single chain variable region fragment of an antibody and a disulfide stabilized variable region.

85. A method of claim 80, wherein the ligand binds to a peptide derived from human pIgR (SEQ ID NO:2), selected from the group consisting of: Lys487-Arg603, Lys487-Glu607, Lys487-Val611, Lys487-Arg615, Lys487-Ala618, Cys520-Arg603, Cys520-Glu607, Cys520-Val611, Cys520-Arg615, Cys520-Ala618, Lys577-Arg603, Lys577-Glu607, Lys577-Val611, Lys577-Arg615, Lys577-Ala618, Ser574-Arg603, Ser574-Glu607, Ser574-Val611, Ser574-Arg615, Ser574-Ala618, Val560-Arg603, Val560-Glu607, Val560-Val611, Val560-Arg615, Val560-Ala618, Cys544-Arg603, Cys544-Glu607, Cys544-Val611, Cys544-Arg615, and Cys544-Ala618.

86. The method of claim 80, wherein the ligand binds to an epitope of pIgR selected from the group consisting of QDPRLF (SEQ ID NO:10), LDPRLF (SEQ ID NO:11), KAIQDPRLF (SEQ ID NO:12), LDPRLFADERI (SEQ ID NO:13), DENKANLDPRLF (SEQ ID NO:14), RLFADEREI (SEQ ID NO:15), and LDPRLFADE (SEQ ID NO:16).

87. A method of claim 80, wherein the ligand is further defined as having a binding component for selectively binding to a region of pIgR and a biologically active component.

88. A method of claim 87, wherein said biologically active component is selected from the group consisting of a nucleic acid, a peptide, a protein, a radioisotope, a lipid, a carbohydrate, a peptidomimetic, an anti-inflammatory, an antisense oligonucleotide, an antibiotic, and an anti-infective.

89. A method of claim 87, wherein said biologically active component is a small molecule.

90. A method of claim 80, wherein the animal is a mammal.

91 A method of claim 90, wherein the cell is a mammalian cell.

92. A method of claim 91, wherein the cell is an epithelial cell.

93. A method of increasing the rate by which a first ligand which binds to secretory component (SC) is transcytosed from an apical to a basolateral side of a cell of an organ of interest in an animal, which cell expresses a polymeric immunoglobulin

receptor (pIgR) from an apical surface by

(a) binding the pIgR at the apical side of said cell with a second ligand, which second ligand inhibits proteolytic cleavage of SC by at least one-third, and further which second ligand does not substantially bind to a stalk remaining attached to the cell after proteolytic cleavage, and

(b) binding the first ligand to the SC,

thereby permitting transcytosis of the SC to which the first ligand has bound from the apical to the basolateral side of said cell.